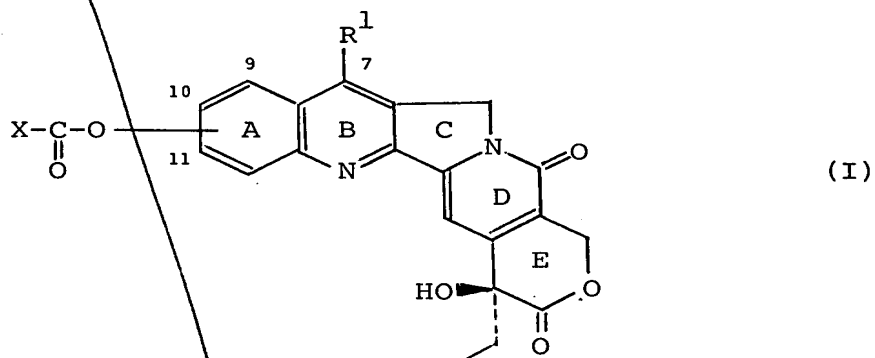


WHAT IS CLAIMED IS:

1. New camptothecin derivatives of the general formula:

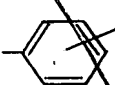
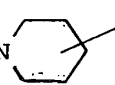


wherein  $R^1$  is a hydrogen atom, a halogen atom or an alkyl group with 1-4 carbon atoms and X is a chlorine atom or  $-NR^2R^3$  where  $R^2$  and  $R^3$  are the same or different and each represents a hydrogen atom, a substituted or unsubstituted alkyl group with 1-4 carbon atoms or a substituted or unsubstituted carbocyclic or heterocyclic group, with the proviso that when both  $R^2$  and  $R^3$  are the substituted or unsubstituted alkyl groups, they may be combined together with the nitrogen atom, to which they are bonded, to form a heterocyclic ring which may be interrupted with  $-O-$ ,  $-S-$  and/or  $>N-R^4$  in which  $R^4$  is a hydrogen atom, a substituted or unsubstituted alkyl group with 1-4 carbon atoms or a substituted or unsubstituted phenyl group and wherein the grouping  $-O-CO-X$  is bonded to a carbon atom located in any of the 9-, 10- and 11-positions in the ring A, as well as an ammonium salt or an alkali metal salt thereof.

2. New camptothecin derivatives according to claim 1, wherein  $R^2$ ,  $R^3$  or  $R^4$  in case of the alkyl group is substituted by one or more substituents selected from the following atoms and/or groups:

- (A)  $-F$ ,  $-Cl$ ,  $-Br$  and  $-I$ ,  
 (B)  $-OH$  and  $-OR^5$ ,

(C)  $-\text{COOR}^6$ ,  $-\text{SO}_3\text{R}^6$  and  $-\text{PO}_3(\text{R}^6)_2$ ,

(D)   $(\text{R}^7)_n$  and   $(\text{R}^7)_n$ ,

(E)  $-\text{NR}^8\text{R}^9$  and  $-\text{CONR}^8\text{R}^9$ , and

(F)  $-\text{Q}-\text{A}-\text{OR}^5$ ,  $-\text{Q}-\text{A}-\text{NR}^8\text{R}^9$  and  $-\text{Q}-\text{A}-\text{Q}-\text{R}^5$

5 wherein  $\text{R}^5$  is an alkyl group with 1-4 carbon atoms or a phenyl  
group which may be substituted by a halogen atom or an alkyl  
group with 1-4 carbon atoms,  $\text{R}^6$  is a hydrogen atom or an alkyl  
group with 1-4 carbon atoms,  $\text{R}^7$  is a hydrogen atom, a halogen  
atom, an alkyl group with 1-4 carbon atoms or an alkoxy group  
10 with 1-4 carbon atoms,  $n$  is an integer of 1-3,  $\text{R}^8$  and  $\text{R}^9$  are  
the same or different and each represents a hydrogen atom or  
an alkyl group with 1-4 carbon atoms with the proviso that when  
both  $\text{R}^8$  and  $\text{R}^9$  are the alkyl groups, they may be combined together  
with the nitrogen atom, to which they are bonded, to form a  
15 heterocyclic group which may be interrupted with  $-\text{O}-$ ,  $-\text{S}-$  or  
 $>\text{N}-\text{R}^6$ ,  $\text{Q}$  is the grouping  $-\text{O}-\text{CO}-$  or  $-\text{CO}-\text{O}-$ , and  $\text{A}$  is a straight or  
branched chain alkylene group with 1-4 carbon atoms.

3. ~~9-Chlorocarbonyloxy-7- $\text{R}^1$ -camptothecins.~~

4. ~~10-Chlorocarbonyloxy-7- $\text{R}^1$ -camptothecins.~~

5. ~~11-Chlorocarbonyloxy-7- $\text{R}^1$ -camptothecins.~~

6. ~~9-[ $\text{N}-\text{R}^8-\text{N}-(\text{R}^8\text{R}^9\text{amino})\text{C}_{1-4}$ -alkyl]carbonyloxy-7- $\text{R}^1$ -camptothecins~~

7. ~~9-(4- $\text{R}^4$ -piperazino)carbonyloxy-7- $\text{R}^1$ -camptothecins.~~

8. ~~9-( $\text{R}^8\text{R}^9\text{N}-\text{C}_{1-4}$ -alkyl)carbonyloxy-7- $\text{R}^1$ -camptothecins.~~

9. ~~9-[4-(1-piperidino)-1-piperidino]carbonyloxy-7- $\text{R}^1$ -  
25 camptothecins.~~

10. ~~10- $\text{C}_{1-4}$ -alkylaminocarbonyloxy-7- $\text{R}^1$ -camptothecins.~~

11. ~~10-(di- $\text{C}_{1-4}$ -alkylamino)carbonyloxy-7- $\text{R}^1$ -camptothecins.~~

12. ~~10-(4- $\text{R}^4$ -piperazino)carbonyloxy-7- $\text{R}^1$ -camptothecins.~~

13. ~~10-( $\text{R}^8\text{R}^9\text{N}-\text{C}_{1-4}$ -alkyl)carbonyloxy-7- $\text{R}^1$ -camptothecins.~~

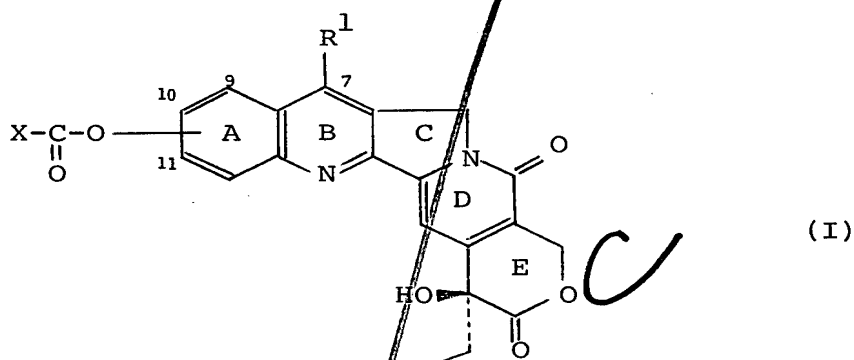
14. 10-[4-(1-piperidino)-1-piperidino]carbonyloxy-7-R<sup>1</sup>-camptothecins.

15. 11-[N-C<sub>1-4</sub> alkyl-N(R<sup>8</sup>R<sup>9</sup> amino)C<sub>1-4</sub> alkyl]carbonyloxy-7-R<sup>1</sup>-camptothecins.

16. 11-(4-R<sup>4</sup>-piperazino)carbonyloxy-7-R<sup>1</sup>-camptothecins.

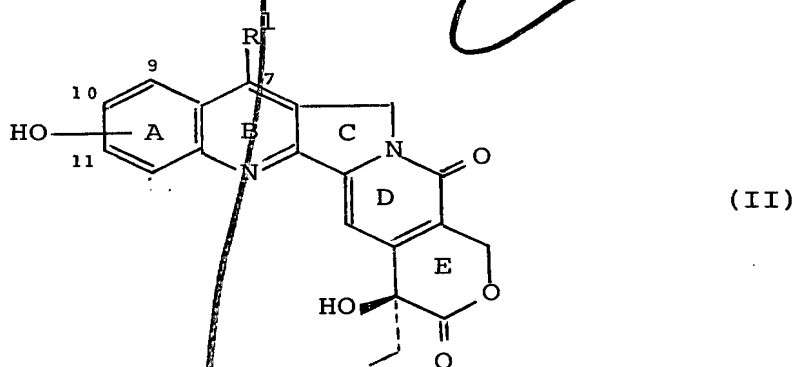
17. 11-[4-(1-piperidino)-1-piperidino]carbonyloxy-7-R<sup>1</sup>-camptothecins.

18. A process for the preparation of new camptothecin derivatives of the general formula:

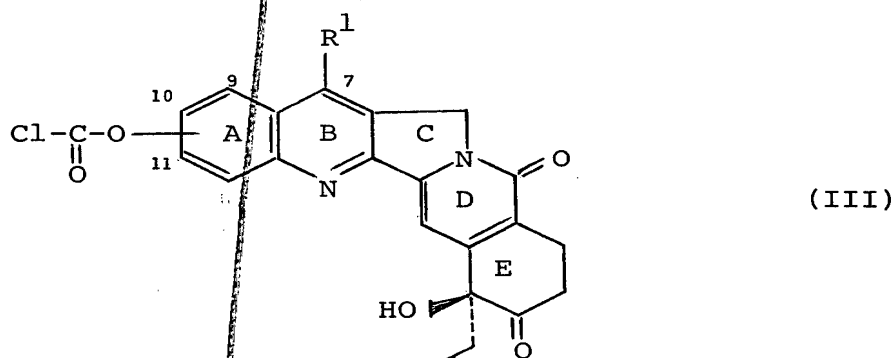


wherein R<sup>1</sup> is a hydrogen atom, a halogen atom or an alkyl group with 1-4 carbon atoms and X is a chlorine atom or -NR<sup>2</sup>R<sup>3</sup> where R<sup>2</sup> and R<sup>3</sup> are the same or different and each represents a hydrogen atom, a substituted or unsubstituted alkyl group with 1-4 carbon atoms or a substituted or unsubstituted carbocyclic or heterocyclic group, with the proviso that when both R<sup>2</sup> and R<sup>3</sup> are the substituted or unsubstituted alkyl groups, they may be combined together with the nitrogen atom, to which they are bonded, to form a heterocyclic ring which may be interrupted with -O-, -S- and/or >N-R<sup>4</sup> in which R<sup>4</sup> is a hydrogen atom, a substituted or unsubstituted alkyl group with 1-4 carbon atoms or a substituted or unsubstituted phenyl group and wherein the grouping -O-CO-X is bonded to a carbon atom located in any of the 9-, 10- and 11-

positions in the ring A,  
as well as ammonium salts or alkali metal salts thereof,  
which comprises reacting a hydroxycamptothecin derivative of the  
general formula:



- 5 wherein  $R^1$  has the same meaning as given above and the hydroxy group OH is bonded to a carbon atom located in any of the 9-, 10- and 11-positions in the ring A,  
with phosgen to form a chlorocarbonyloxycamptothecin derivative of the general formula:



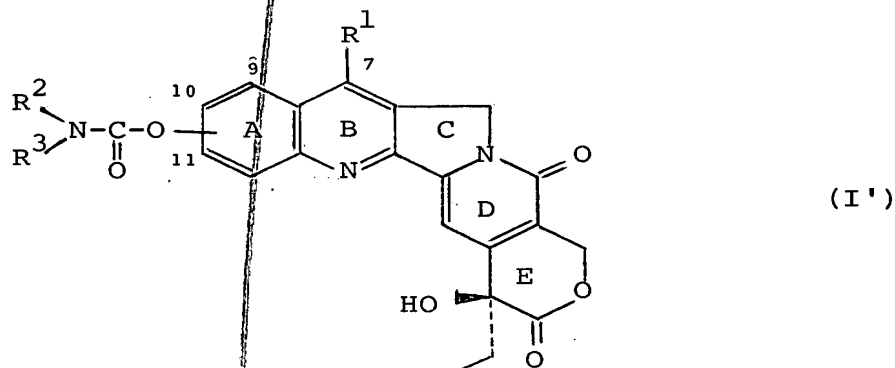
- 10 wherein  $R^1$  has the same meaning as given above and the grouping Cl-CO-O- is bonded to a carbon atom located in any of the 9-, 10- and 11-positions in the ring A,  
and, if necessary, treating the chlorocarbonyloxycamptothecin derivative with an amine of the general formula:



wherein  $R^2$  and  $R^3$  have the same meaning as given above,  
 and if desired, converting  $R^2$  and/or  $R^3$  in the resultant amino-  
 carbonyloxycamptothecin derivative of the general formula (I)  
 where X is  $-N\begin{smallmatrix} R^2 \\ R^3 \end{smallmatrix}$  into another  $R^2$  and/or  $R^3$  by N-alkylation or  
 5 O-alkylation according to the method known per se and/or convert-  
 ing the resultant aminocarbonyloxycamptothecin derivative into  
 an ammonium salt thereof with an acid or into an alkali metal  
 salt thereof with a strong alkali metal base.

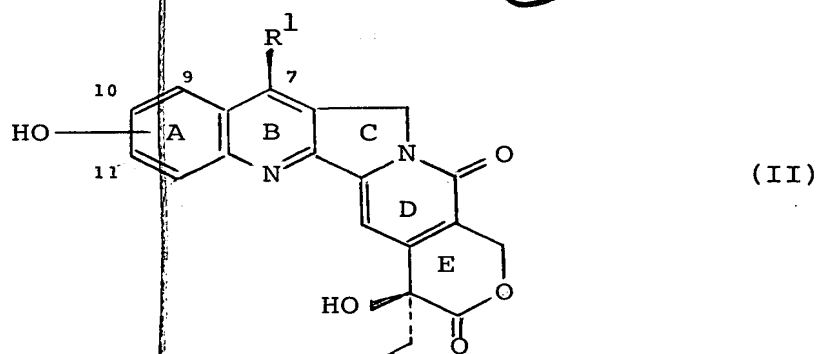
19. A process according to claim 18, wherein the reaction  
 10 is carried out in the presence of an anhydrous solvent and  
 an acid-binding agent.

20. A process for the preparation of new camptothecin  
 derivatives of the general formula:



wherein  $R^1$  is a hydrogen atom, a halogen atom or an alkyl group  
 15 with 1-4 carbon atoms and  $R^2$  and  $R^3$  are the same or different  
 and each represents a hydrogen atom, a substituted or unsubsti-  
 tuted alkyl group with 1-4 carbon atoms or a substituted or  
 unsubstituted carbocyclic or heterocyclic group with the proviso  
 that when both  $R^2$  and  $R^3$  are the substituted or unsubstituted  
 20 alkyl groups, they may be combined together with the nitrogen  
 atom, to which they are bonded, to form a heterocyclic ring  
 which may be interrupted with -O-, -S- and/or  $>N-R^4$  in which  
 $R^4$  is a hydrogen atom, a substituted or unsubstituted alkyl group

with 1-4 carbon atoms or a substituted or unsubstituted phenyl group and wherein the grouping  $-O-CO-N\begin{smallmatrix} R^2 \\ R^3 \end{smallmatrix}$  is bonded to a carbon atom located in any of the 9-, 10- and 11-positions in the ring A, as well as ammonium salts or alkali metal salts thereof, which comprises reacting a hydroxycamptothecin of the general formula:



wherein  $R^1$  has the same meaning as given above and the hydroxy group OH is bonded to a carbon atom located in any of the 9-, 10- and 11-positions in the ring A, with a carbamoyl chloride of the general formula:



wherein  $R^2$  and  $R^3$  have the same meanings as given above, and if desired, converting  $R^2$  and/or  $R^3$  in the resultant aminocarbonyloxycamptothecin derivative of the general formula (I') into another  $R^2$  and/or  $R^3$  by O-alkylation or N-alkylation according to the method known per se and/or converting the resultant aminocarbonyloxycamptothecin derivative into an ammonium salt thereof with an acid or into an alkali metal salt thereof with a strong alkali metal base.

21. A process according to claim 20, wherein the reaction is carried out in the presence of an aprotic solvent and an acid-binding agent.

22. A process according to claim 20, wherein the carbamoyl chloride is used in a theoretical excess amount.

*Add Ba*